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- (51) International Patent Classification⁷: C12N 15/11, A61K 31/70, A61P 31/04 (74) Agent: MBM & CO.; P.O. Box 809, Station B, Ottawa, Ontario K1P 5P9 (US).
- (21) International Application Number: PCT/CA00/01347 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
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- (30) Priority Data: 60/166,249 18 November 1999 (18.11.1999) US
- (71) Applicant (*for all designated States except US*): GENE-SENSE TECHNOLOGIES, INC. [CA/CA]; 7100 Woodbine Avenue, Suite 215, Markham, Ontario L3R 5J2 (CA).
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- (75) Inventors/Applicants (*for US only*): WRIGHT, Jim, A. [CA/CA]; 49 Golf Links Drive, Aurora, Ontario L4G 3V4 (CA). YOUNG, Aiping, H. [CA/CA]; 201 Senlac Road, North York, Ontario M2R 1P3 (CA). DUGOURD, Dominique [CA/CA]; 1053A Mount Pleasant Road, Toronto, Ontario M4P 2M5 (CA).
- Published:
— with international search report
- (88) Date of publication of the international search report:
10 January 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: ANTISENSE OLIGONUCLEOTIDE SEQUENCES DERIVED FROM *groEL* AND *groES* AS INHIBITORS MICROORGANISMS

(57) Abstract: The present invention provides antisense oligonucleotides which modulate the expression of the *groEL* or *groES* genes in microorganisms. This invention is also related to methods of using such oligonucleotides in inhibiting the growth of microorganisms. These antisense oligonucleotides are particularly useful in treating pathological conditions in mammals which are mediated by the growth of microorganisms.

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PATENT COOPERATION TREATY

PCT

9/786212

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 683-114PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 01347	International filing date (day/month/year) 20/11/2000	(Earliest) Priority Date (day/month/year) 18/11/1999
Applicant GENESENSE TECHNOLOGIES, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

ANTISENSE OLIGONUCLEOTIDE SEQUENCES DERIVED FROM GROEL AND GROEL AS INHIBITORS MICROORGANISMS

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

Inter nal Application No

PCT/CA 00/01347

A. CLASSIFICATION OF SUBJECT-MATTER

IPC 7 C12N15/11 A61K31/70 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	<p>WO 98 03533 A (OLIGOS ETC. AND OLIGOS THERAPEUTICS, INC.) 29 January 1998 (1998-01-29)</p> <p>abstract</p> <p>page 8, line 1 -page 17, line 11 page 19, line 1 -page 37, line 9 page 42, line 18 -page 48, line 3 page 51, line 18 -page 57, line 15 page 60, line 9 -page 66, line 29 page 75, line 26 -page 76, line 28 NBT 66 (SEQ ID NO: 22) page 82; table 1 page 132 -page 139; claims 1-78 ---</p> <p>-/--</p>	<p>1,2, 4-14,27, 28,30, 32,33, 36,37,40 3,15-26, 29,31, 34,35, 38,39</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 June 2001

Date of mailing of the international search report

17. 9. 01

Name and mailing address of the ISA

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Authorized officer

Fuchs, U

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01347

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 945 290 A (COWSERT, L.M.) 31 August 1999 (1999-08-31) the whole document	1-40
A	HEMMINGSEN, S.M. ET AL.: "Homologous plant and bacterial proteins chaperone oligomeric protein assembly" NATURE, vol. 333, no. 6171, 26 May 1988 (1988-05-26), pages 330-334, XP002114158 cited in the application see especially: page 331; figure 1 page 334, column 1, line 31 -column 2, line 10 the whole document	1-40
A	IVIC, A. ET AL.: "Deletion of Escherichia coli groEL is complemented by a Rhizobium leguminosarum groEL homologue at 37 C but not at 43 C" GENE, vol. 194, no. 1, 18 July 1997 (1997-07-18), pages 1-8, XP004084653 cited in the application the whole document	1-40

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 00/01347

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 40 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-40 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-40 partially

Invention 1

An antisense compound 5 to 50 nucleobases in length targeted to a nucleic acid molecule encoding groEL or groES of a microorganism specifically hybridizing with and inhibiting the expression of groEL or groES, a composition comprising said antisense compound and a pharmaceutically acceptable carrier or diluent, a method of inhibiting the expression of groEL or groES in cells or tissues in vitro comprising contacting said cells or tissues with said antisense compound, an antisense compound up to 50 nucleobases in length targeted to a nucleic acid molecule encoding groEL or groES comprising at least a 5 nucleobase portion of SEQ ID NO: 16, a composition comprising said antisense compound and a pharmaceutically acceptable carrier or diluent, a method of inhibiting the expression of groEL or groES in cells or tissues in vitro comprising contacting said cells or tissues with said antisense compound, an antisense oligonucleotide comprising 5 to 50 nucleotides which are complementary to the groEL or groES gene of a microorganism, a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of said antisense oligonucleotide, a method of inhibiting the expression of a groEL or groES gene in a microorganism comprising administering to said microorganism or to a cell infected with said microorganism an effective amount of said antisense oligonucleotide, an antisense oligonucleotide comprising 5 to 50 nucleotides being capable of binding to the groEL or groES gene of a microorganism and comprising all or part of the sequence SEQ ID NO: 16, a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of said antisense oligonucleotide, a method of inhibiting the growth of a microorganism comprising identifying said microorganism and administering to said microorganism an effective amount of an antisense oligonucleotide comprising at least 5 nucleotides being complementary to either the groEL or groES gene of said microorganism;

2. Claims: 1-40 partially

Invention 2

Idem as subject 1 but limited to SEQ ID NO: 17;

3.-465. Claims: 1-40 partially

Inventions 3-465

Idem as subject 1 but limited to SEQ ID NOS: 18-480

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(corresponding to Tabs. 1-4 of the description).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/01347

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9803533 A	29-01-1998	AU 3811897 A	10-02-1998
US 5945290 A	31-08-1999	AU 3868699 A	10-04-2000
		WO 0017223 A	30-03-2000